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(54) Cosmetic composition.

(57) A smectic mesophase formed in vitro comprising two or more lipids wherein the lipids together form a smectic mesophase having a repeat distance (d/o) of greater than 90Å, the individual lipid components having a d/o of less than 70Å, and its use within a cosmetic composition suitable for topical application to skin, hair or nails.

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R_1 and R_2 individually represent hydrogen or a carbonyl.
A to K represent the bond between specified carbon atoms, these may be saturated or unsaturated.
Wherein the hydroxyl group on carbon 3 is in the β configuration.

The Sterol Component

R is preferably a C_{1-16} alkyl chain, more preferably a C_{1-10} alkyl chain, most preferably a C_{5-10} alkyl chain.

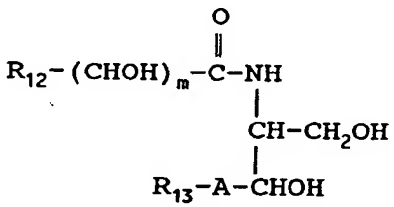
Preferably sterols having the general structure (1) are selected from cholesterol, pro-vitamin D_3 (7-dehydrocholesterol), campesterol, stigmastanol, stigmasterol, 5-dihydrocholesterol, α-spinasterol, palysterol, clionasterol, γ-sitosterol, stigmasten-3β-ol, sargasterol, avenasterol, ergostanol, β-sitosterol, corbisterol, chondrillasterol, poriferasterol, haliclonaseterol, neospongosterol, fucosterol, aptostanol, ergostadien-3β-ol, pro-vitamin D_2 (ergosterol), 22-dihydroergosterol, brassicasterol, 24-methylenecholesterol, 5-dihydroergosterol, dehydroergosterol, 14-dehydroergosterol, 24-dehydroergosterol, fungisterol, cholestanol, coprostanol, zymosterol, 7-ketocholesterol, lathosterol, 22-dehydrocholesterol, β-sitosterol, cholestatrien-3β-ol, coprostonal, cholestanol, ergosterol, 24-dehydrocholest-adione-3β-ol, dihydrositosterol, stigmastan-3β-ol, cholestan-3β-ol, cholestan-3β-ol-6-one , di-hydroergosterol, brassicasterol, 24-methylenecholesterol, 5-dihydroergosterol, episterol, acosterol, fecosterol, 14-dehydroergosterol, dehydroergosterol, and mixtures thereof.

More preferably the sterol is selected from cholesterol, 7-dehydrocholesterol, 5-dihydrocholesterol capesterol, ergosterol, stigmastanol, stigmasterol, and mixtures thereof.

Even more preferably the sterol is cholesterol.

The Ceramide Component

The ceramide component is preferably selected from ceramides having the general structure (2),

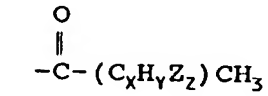


(2)

where A represents $-CH_2$ or -CH=CH- or -CHOQ-.

R_{12} represents a linear or branched, saturated or unsaturated, hydroxylated or non-hydroxylated aliphatic hydrocarbon group having from 8 to 28 carbon atoms.

R_{13} represents a linear or branched, saturated or unsaturated, hydroxylated or non-hydroxylated aliphatic hydrocarbon having from 8 to 28 carbon atoms.
m is 0 or 1
Q represents H or a residue of a C_{14} to C_{22} fatty acid having the structure (3)



(3)

Z is -OH or an epoxy oxygen
x is an integer of from 12 to 20
y is an integer of from 20 to 40
z is 0 or an integer of from 1 to 4.

More preferably the ceramide component is a ceramide having the general structure (2) selected from;
Ceramide 2 having the structure (4)

Since skin contains both sterol and ceramides, it is possible to form the smectic mesophase in vitro from extracted skin lipids.

Preferably the lipid components

(a) ceramide; and

(b) sterol having the general structure (1)

are present within the smectic mesophase such that the mole ratio of (a):(b) is 1:0.05 to 1:1.

More preferably the mole ratio of (a):(b) is 1:0.25 to 1:1.

Even more preferably the mole ratio of (a):(b) is 1:1.

METHOD OF FORMING THE SMECTIC MESOPHASE

The smectic mesophase may be formed using one of two methods.

Method One

(i) heat lipid components until melted (≧90°C)

(ii) mix components

(iii) cool to room temperature

Method Two

(ia) dissolve lipids in suitable solvent, for example acetone, chloroform:methanol, methanol, ethanol.

(iia) mix

(iiia) evaporate solvent

DISCLOSURE OF THE COMPOSITION

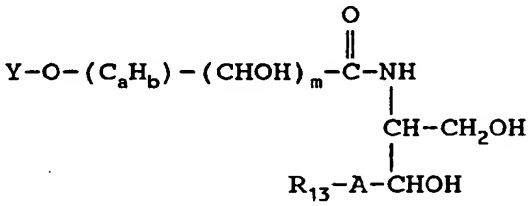
The composition according to the invention comprises in its simplest form

(a) a smectic mesophase formed in vitro comprising two or more lipids wherein the lipids together form a smectic mesophase having a repeat distance (d/o) of greater than 90Å, the individual lipid components having a d/o of less than 70Å .

(b) a cosmetically acceptable vehicle for the lipid containing smectic mesophase.

The amount of the lipid formed into the smectic mesophase present in the composition according to the invention is from 0.00001 to 50%, preferably from 0.001 to 20% and most preferably from 0.1 to 10% by weight.

The composition according to the invention may additionally comprise a lipid component which does not form part of the smectic mesophase. Preferably this additional lipid component is selected from ceramide, including ceramides having the general structure (7), pseudoceramides including pseudoceramides having the general structure (9), sterols and mixtures thereof.



(7)

Where A represents $-CH_2-$, $-CH=CH-$ or $-CHOH-$,

R_{13} represents a linear or branched, saturated or unsaturated, hydroxylated or non-hydroxylated aliphatic hydrocarbon having from 8 to 28 carbon atoms.

a is an integer of from 7 to 49

b is an integer of from 10 to 98

m is 0 or 1

Y represents H or a residue of a C_{14} to C_{22} fatty acid having the structure (8)

The Cosmetically Acceptable Vehicle

The composition according to the invention also comprises a cosmetically acceptable vehicle to act as a dilutant, dispersant or carrier for the lipid containing smectic mesophase in the composition, so as to facilitate its distribution when the composition is applied to the skin and/or hair.

Vehicles other than water can include liquid or solid emollients, solvents, humectants, thickeners and powders. Examples of each of these types of vehicle, which can be used singly or as mixtures of one or more vehicles, are as follows:

Emollients, such as stearyl alcohol, glyceryl monoricinoleate, glyceryl monostearate, mink oil, cetyl alcohol, isopropyl isostearate, stearic acid, isobutyl palmitate, isocetyl stearate, oleyl alcohol, isopropyl laurate, hexyl laurate, decyl oleate, octadecan-2-ol, isocetyl alcohol, eicosanyl alcohol, behenyl alcohol, cetyl palmitate, silicone oils such as dimethylpolysiloxane, din-butyl sebacate, isopropyl myristate, isopropyl palmitate, isopropyl stearate, butyl stearate, polyethylene glycol, triethylene glycol, lanolin, cocoa butter, corn oil, cotton seed oil, tallow, lard, olive oil, palm kernel oil, rapeseed oil, safflower seed oil, evening primrose oil, soybean oil, sunflower seed oil, avocado oil, olive oil, sesame seed oil, coconut oil, arachis oil, castor oil, acetylated lanolin alcohols, petroleum jelly, mineral oil, butyl myristate, isostearic acid, palmitatic acid, isopropyl linoleate, lauryl lactate, myristyl lactate, decyl oleate, myristyl myristate;

Propellants, such as air, propane, butane, isobutane, dimethyl ether, carbon dioxide, nitrous oxide;

Solvents, such as ethyl alcohol, methylene chloride, isopropanol, acetone, ethylene glycol monoethyl ether, diethylene glycol monobutyl ether, diethylene glycol monoethyl ether, dimethyl sulphoxide, dimethyl formamide, tetrahydrofuran;

Powders, such as chalk, talc, fullers earth, kaolin, starch, gums, colloidal silica sodium polyacrylate, tetra alkyl and/or trialkyl aryl ammonium smectites, chemically modified magnesium aluminium silicate, organically modified montmorillonite clay, hydrated aluminium silicate, fumed silica, carboxyvinyl polymer, sodium carboxymethyl cellulose, ethylene glycol monostearate.

The cosmetically acceptable vehicle will usually form from 10 to 99.9%, Preferably from 50 to 99% by weight of the emulsion, and can, in the absence of other cosmetic adjuncts, form the balance of the composition.

OPTIONAL SKIN BENEFIT MATERIALS AND COSMETIC ADJUNTS

A particularly convenient form of the composition according to the invention is an emulsion, in which case an oil or oily material will normally be present, together with an emulsifier to provide either a water-in-oil emulsion or an oil-in-water emulsion, depending largely on the average hydrophilic-lyophilic balance (hlb) of the emulsifier employed.

Oil or oily material

The composition according to the invention can optionally comprise one or more oils or other materials having the properties of an oil.

Examples of suitable oils include mineral oil and vegetable oils, and oil materials, such as those already proposed herein as emollients. Other oils or oily materials include silicone oils, both volatile and non-volatile, such as polydimethyl siloxanes.

The oil or oily material, when present for the purposes for forming an emulsion, will normally form up to 90%, preferably from 10 to 80% by volume of the composition.

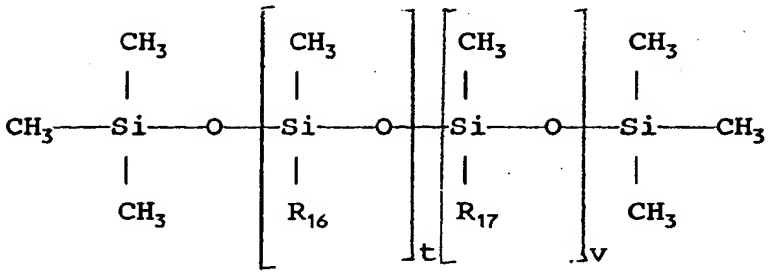
Emulsifier

The composition according to the invention can also optionally comprise one or more emulsifiers the choice of which will normally determine whether a water-in-oil or and oil-in-water emulsion is formed.

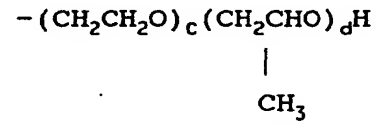
When a water-in-oil emulsion is required, the chosen emulsifier or emulsifiers should normally have an average HLB value of from 1 to 6. When an oil-in-water emulsion is required, a chosen emulsifier or emulsifiers should have an average HLB value of >6.

Examples of suitable emulsifiers are set below in Table 1 in which the chemical name of the emulsifiers is given together with an example of a trade name as commercially available, and the average HLB value.

Polyoxyethylene (5) monostearate	Ethofat 60-16	9.0
Polyoxyethylene (4) sorbitan monostearate	Tween 61	9.6
Polyoxyethylene (4) lauryl ether	Brij 30	9.7
Polyoxyethylene (5) sorbitan monooleate	Tween 81	10.0
PEG 300 monooleate	Neutronyx 834	10.4
Polyoxyethylene (20) sorbitan tristearate	Tween 65	10.5
Polyoxyethylene (20) sorbitan trioleate	Tween 85	11.0
Polyoxyethylene (8) monostearate	Myrj 45	11.1
PEG 400 monooleate	Emerest 2646	11.7
PEG 400 monostearate	Tegester PEG 400	11.9
Polyoxyethylene 10 monooleate	Ethofat 0/20	12.2
Polyoxyethylene (10) stearyl ether	Brij 76	12.4
Polyoxyethylene (10) cetyl ether	Brij 56	12.9
Polyoxyethylene (9.3) octyl phenol	Triton X-100	13.0
Polyoxyethylene (4) sorbitan monolaurate	Tween 21	13.3
PEG 600 monooleate	Emerest 2660	13.7
PEG 1000 dilaurate	Kessco	13.9
Polyoxyethylene sorbitol lanolin derivative	G-1441	14.0
Polyoxyethylene (12) lauryl ether	Ethosperse LA-12	14.4
PEG 1500 dioleate	Pegosperse 1500	14.6
Polyoxyethylene (14) laurate	Arosurf HFL-714	14.8



where the groups R_{16} and R_{17} are each chosen from -H, C_{1-18} alkyl and



c has a value of from 9 to 115
d has a value of from 0 to 50
t has a value of from 133 to 673
v has a value of from 25 to 0.25.

Preferably, the dimethyl polysiloxane polymer is one in which:
c has a value of from 10 to 114
d has a value of from 0 to 49
t has a value of from 388 to 402
v has a value of from 15 to 0.75.

One of groups R_{16} and R_{17} being lauryl, and the other having a molecular weight of from 1000 to 5000.

A particularly preferred dimethyl polysiloxane polymer is one in which:
c has the value 14
d has the value 13
t has the value 249
v has the value 1.25

The dimethyl polysiloxane polymer is conveniently provided as a dispersion in a volatile siloxane, the dispersion comprising, for example, from 1 to 20% by volume of the polymer and from 80 to 99% by volume of the volatile siloxane. Ideally, the dispersion consists of a 10% by volume of the polymer dispersed in the volatile siloxane.

Examples of the volatile siloxanes in which the polysiloxane polymer can be dispersed include polydimethyl siloxane (pentamer and/or hexamer).

A particularly preferred silicone surfactant is cyclomethicone and dimethicone copolyol, such as DC 3225C formulation aid available from DOW CORNING. Another is laurylmethicone copolyol, such as DC Q2-5200, also available from Dow Corning.

The amount of silicone surfactant, when present in the composition will normally be up to 25%, preferably from 0.5 to 15% by weight of the emulsion.

Other Cosmetic Adjuncts

Examples of conventional adjuncts which can optionally be employed include preservatives, such as para-hydroxy benzoate esters; antioxidants, such butyl hydroxy toluene; humectants, such as glycerol, sorbitol, 2-pyrrolidone-5-carboxylate, dibutylphthalate, gelatin, polyethylene, glycol, preferably PEG 200-600; buffers, such as lactic acid together with a base such as triethanolamine or sodium hydroxide; surfactants, such as glycerol ethers and other ceramides of synthetic, animal or plant origin including ceramide one; phospholipids; waxes, such as beeswax, ozokerite wax, paraffin wax, plant extracts, such as aloe vera, cornflower, witch hazel, elderflower, cucumber; additional sterols, particularly cholesterol; thickeners; activity enhancers; colourants; perfumes; and sunscreen materials such as ultrafine titanium dioxide and organic sunscreens such as p-aminobenzoic acid and esters thereof, ethylhexyl p-methoxycinnamate, 2-ethoxyethyl p-methoxycinnamate

Example	Mole ratios cholesterol:ceramide II
1	0:1
2	0.098:1
3	0.16:1
4	0.27:1
5	0.37:1
6	0.49:1
7	0.85:1
8	1.6:1

The lamellar spacing of "pure" ceramide II (example 1) was 55Å. This spacing did not change the following cooling in situ from isotropic, suggesting that the stable form was present.

Three changes in the diffraction pattern of ceramide II, occur on the addition of cholesterol in samples measured immediately after cooling from isotropic.

(i) The lamellar d/o reflection reduces from 55Å to 41Å as the cholesterol content is increased in relation to the ceramide to a mole ratio of 1.6:1.

(ii) A new peak evolves at 104Å. This is clear in Example 4 although this peak is clearly visible in Example 2 if the sample is aged over two days. This increases in intensity on further addition of cholesterol. This reflection arises from a layered structure, since d/2 and d/3 are visible, although the former is convoluted with the peak described in (i). Increasing the level of cholesterol does not change the d/o value.

(iii) Example 8 showed no evidence of the 104Å reflection, previously induced at lower cholesterol content, but only the d/o and d/2 in (i).

Figures 1-8 show the results of studies on Examples 1-8 respectively.

Examples 9-13 & Comparative Example A

The effect of various sterols on the small angle diffraction pattern of ceramide II or ceramide IV was studied as follows:

Example	Sterol & ceramide studied in 1:1 mole ratio
9	7-dehydrocholesterol & ceramide IV
10	dihydrocholesterol & ceramide II
11	campesterol & ceramide II
12	stigmastanol & ceramide IV
13	stigmasterol & cermide II
A	5β-cholesten-3α-ol & ceramide II

Results are shown in Figures 9-14 respectively.

A smectic mesophose according to the invention was formed with Examples 9-13. Comparative Example A ilustrates the requirement for the hydroxyl group located on carbon number 3 to be in the β configuration, no smectic mesophase being formed when the hydroxyl group is in the α position (as in 5β-cholesten-3α-ol).

Example 14

This example illustrates a high internal phase water-in-oil emulsion in accordance with the invention.

Initially a smectic mesophase was prepared containing ceramide 2 having the structure (4) and cholesterol in a 1:1 mole ratio.

Secondly a high internal phase water-in-oil emulsion having the following formulation was prepared:

	% w/w
Mineral oil	4
Smectic mesophase as detailed above	0.1
Brij 56*	4
Alfol 16RD*	4
Triethanolamine	0.75
Butane-1,3-diol	3
Xanthan gum	0.3
Preservative	0.4
Perfume	qs
Butylated hydroxy toluene	0.01
Water	to 100

*Brij 56 is cetyl alcohol POE (10)
Alfol 16RD is cetyl alcohol

Example 18

This example illustrates an alcoholic lotion in accordance with the invention.

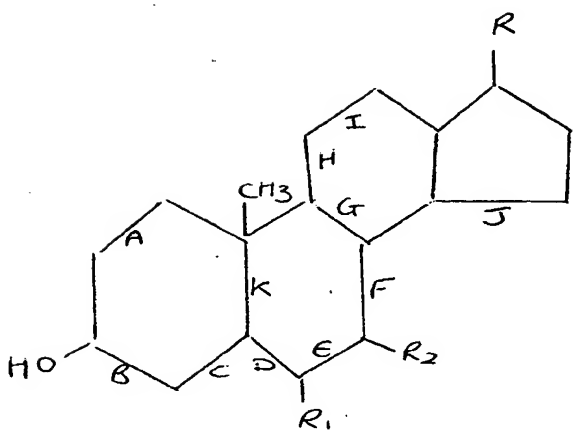
Initially a smectic mesophase was formed form ceramide 2 having the structure (4) and cholesterol in a 1:0.75 mole ratio. Then a lotion was prepared having the following formulation.

	% w/w
Smectic mesophase as detailed above	0.2
Ethanol	40
Perfume	qs
Butylated hydroxy toluene	0.01
Water	to 100

Example 19

The following composition according to the invention represents a lotion which can be used in the treatment of dry skin.

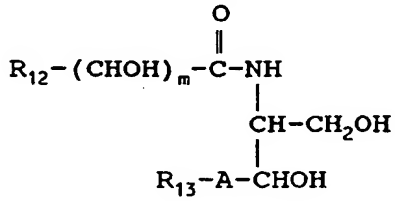
Initially a smectic mesophase was formed from ceramide 2 having the structure (4) and cholesterol in a 1:1 mole ratio. This was then incorporated in the composition as follows:



(1)

where R is a hydroxyl or a C_{1-16} branched/unbranched; saturated/unsaturated alkyl chain;
R_1 and R_2 individually represent H or a carbonyl group;
A to K represent the bond between specified carbon atoms within the sterol structure, these may be saturated or unsaturated; and
wherein the hydroxyl group on carbon 3 is in the β configuration.

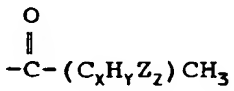
7. A smectic mesophase according to claim 6 wherein the ceramide has the general structure (2):



(2)

where A represents $-CH_2$ or -CH=CH- or -CHOQ-.

R_{12} and R_{13} each individually represents a linear or branched, saturated or unsaturated, hydroxylated or nonhydroxylated aliphatic hydrocarbon group having from 8 to 28 carbon atoms;
m is 0 or 1
q represents H or a residue of a C_{14} to C_{22} fatty acid having the structure (3)



(3)

Z is -OH or an epoxy oxygen
x is an integer of from 12 to 20
y is an integer of from 20 to 40
z is 0 or an integer of from 1 to 4.

8. A smectic mesophase according to claims 6 and 7 wherein the ceramide component is selected from ceramide 2, ceramide 3, ceramide 4, ceramide 5, ceramide 6 (II) and mixtures thereof.

9. A smectic mesophase according to claims 6 to 8 wherein the ceramide component is selected from ceramide 2 and ceramide 4.

10. A smectic mesophase according to claim 6 to 9 wherein the sterol is selected from cholesterol, 7-dehydrocholesterol, campesterol, stigmastanol, stigmasterol, 5-dihydrocholesterol, ergosterol and mixtures thereof.

Fig.1.

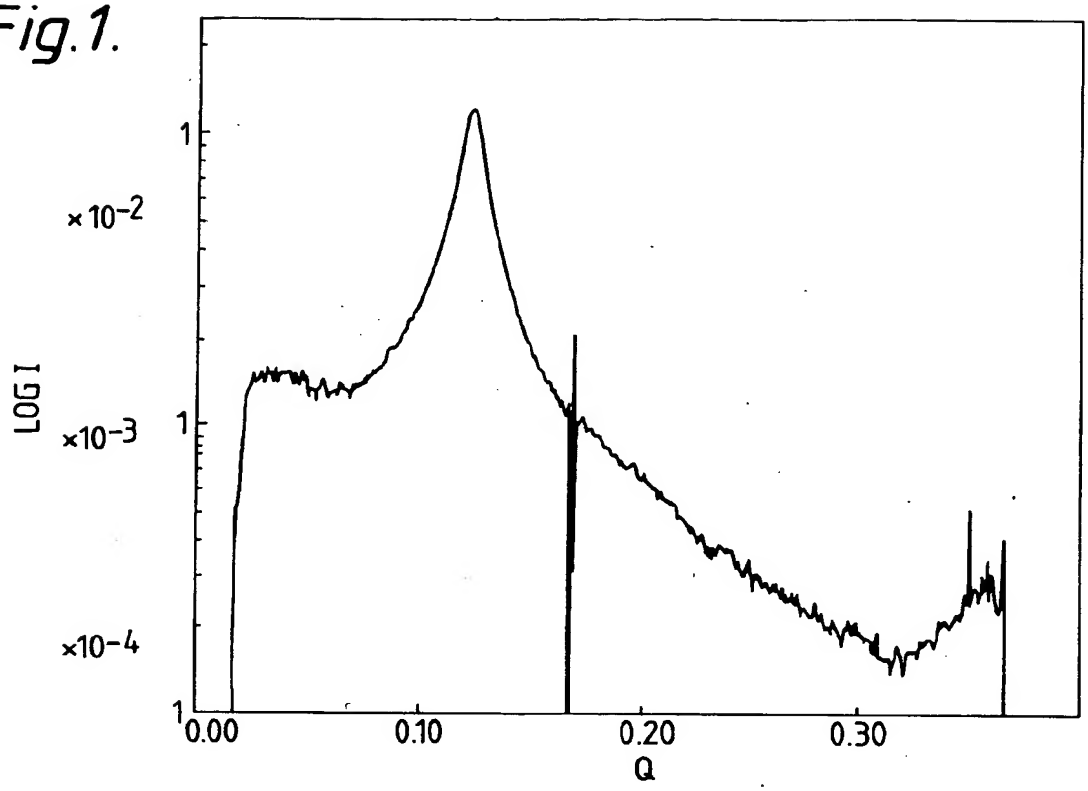


Fig.2.

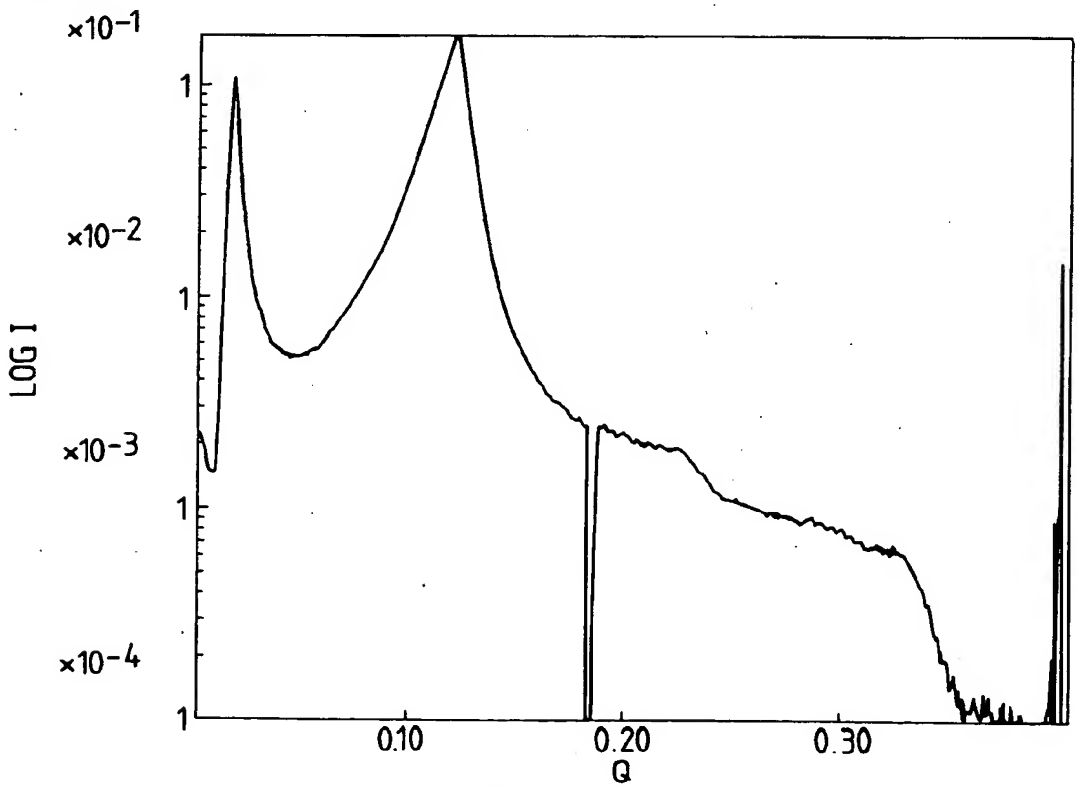


Fig.5.

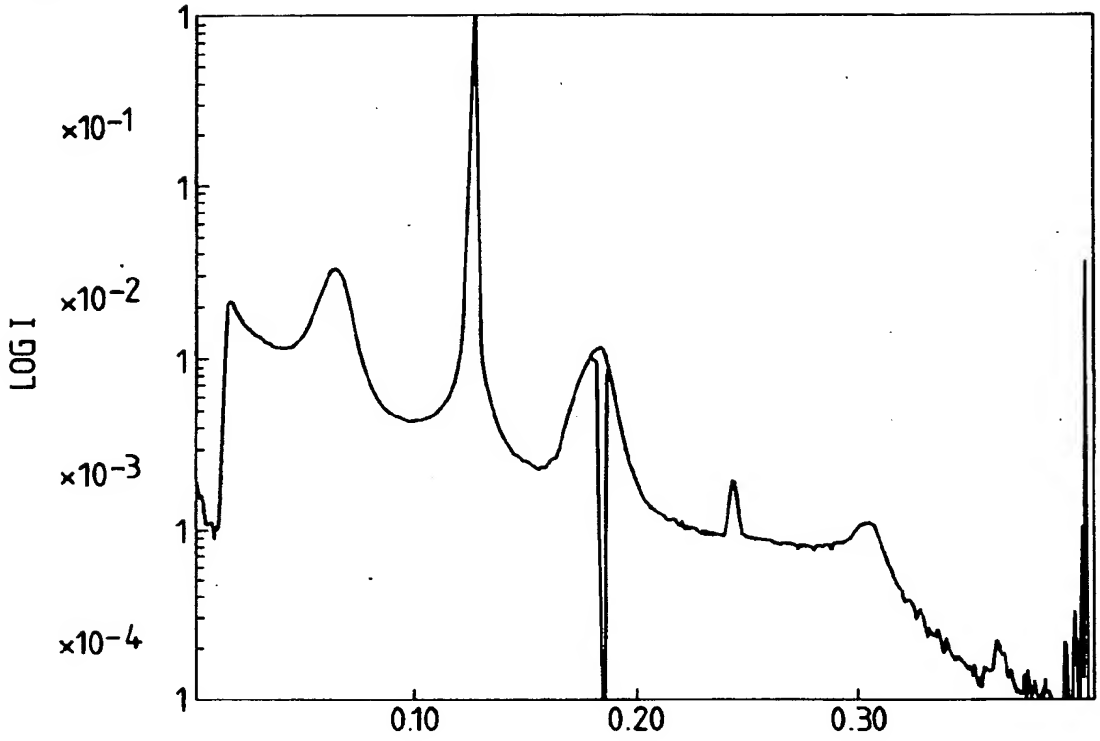


Fig.6.

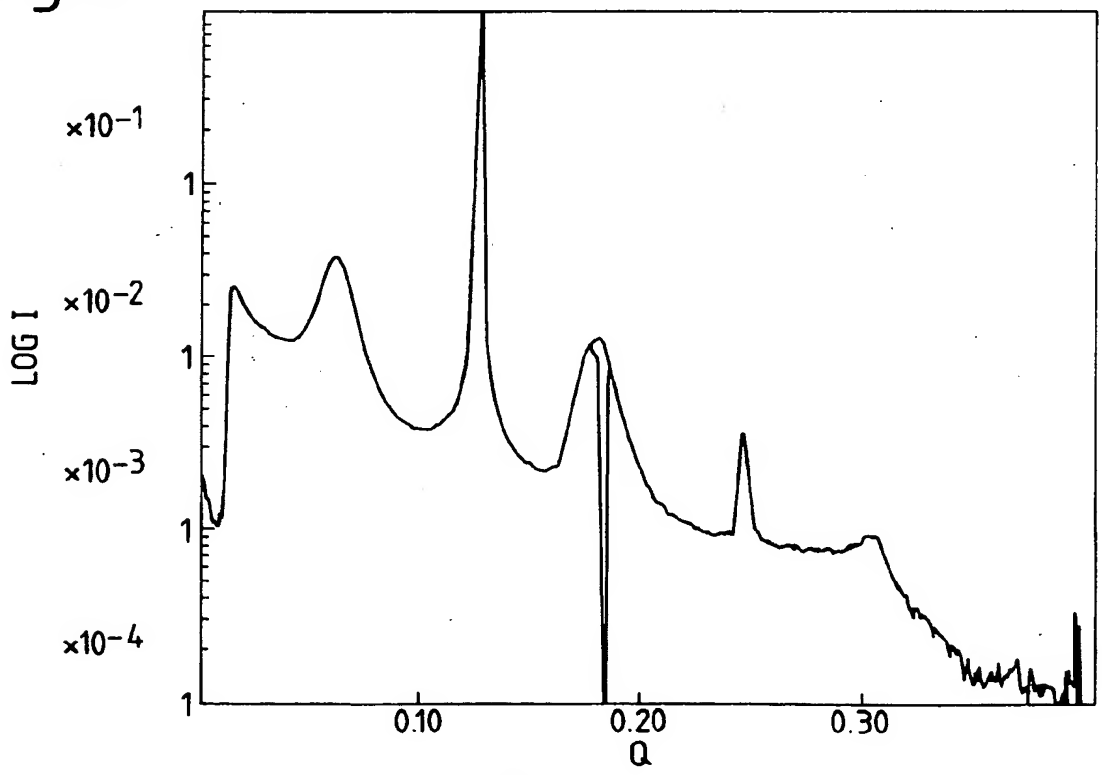


Fig.9.

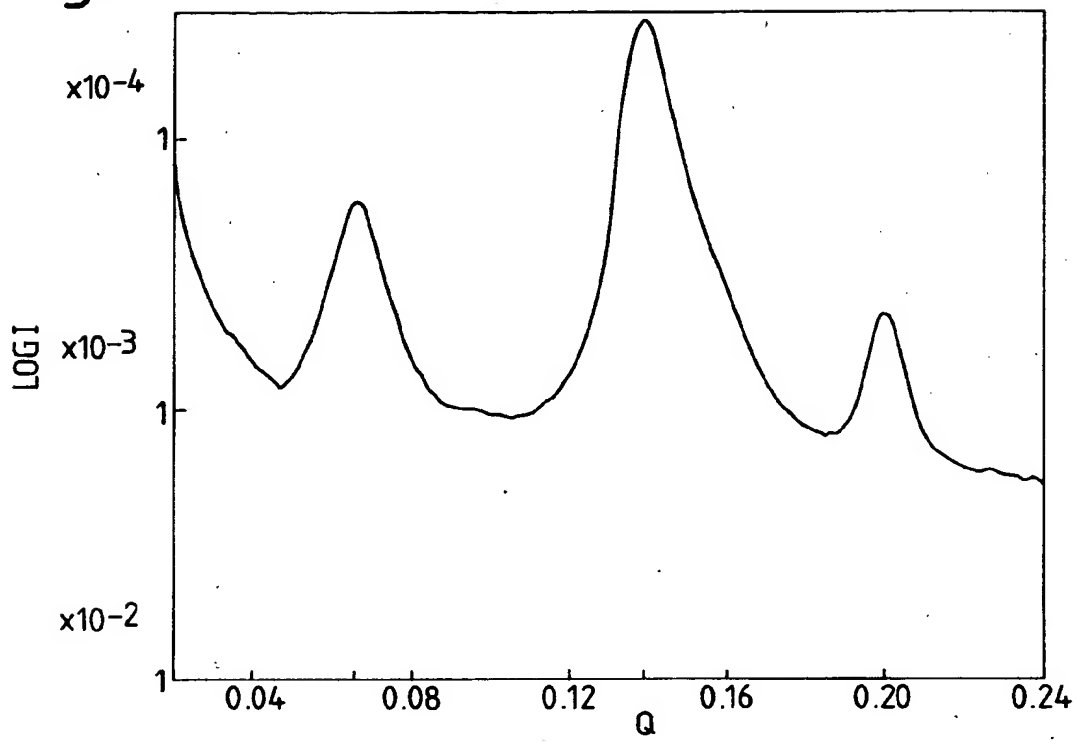


Fig.10.

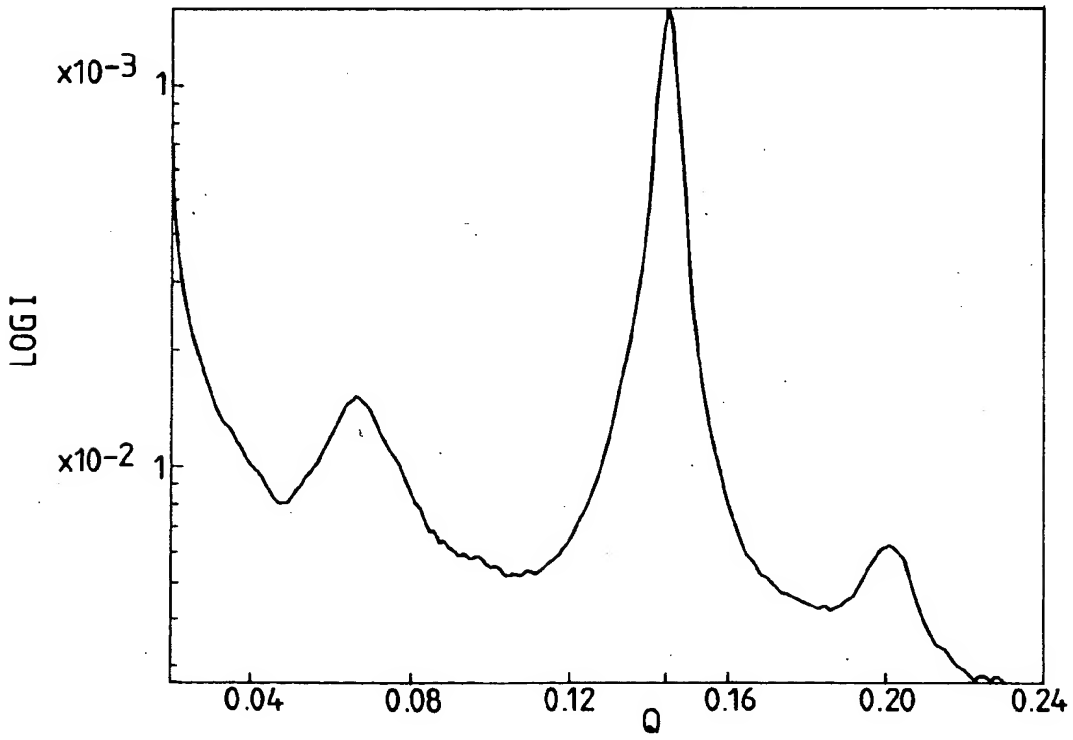


Fig.13.

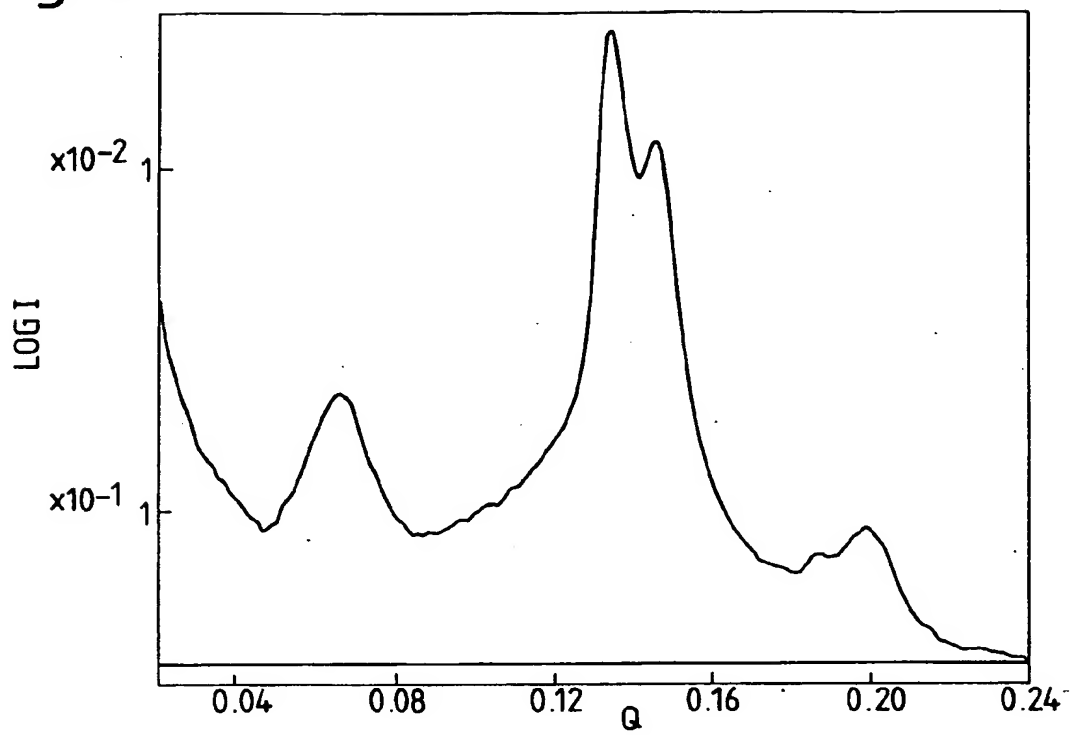
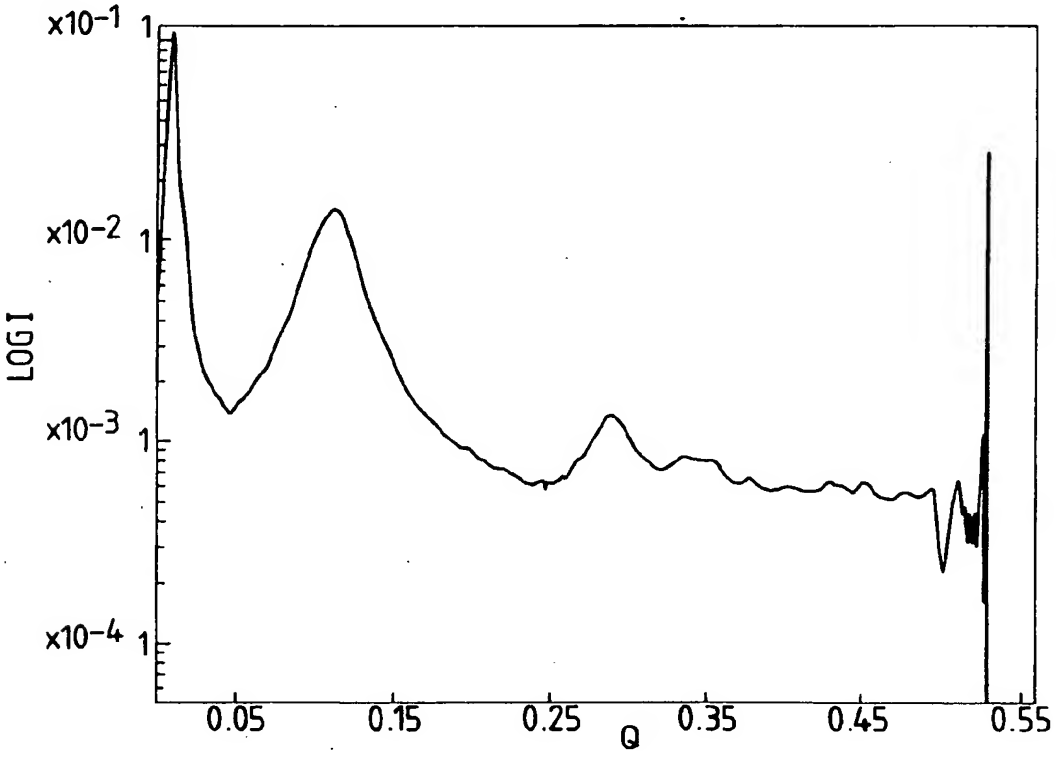


Fig.14.



European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 93 30 7552

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)
Y	EP-A-0 420 722 (L'OREAL) * claims 1-16; example V *	1-19	A61K7/00 A61K9/127
Y	EP-A-0 500 437 (L'OREAL) * claims 1-19; examples 1,2,8 *	1-19	
A	WO-A-91 04013 (MICRO VESICULAR SYSTEMS) * claims 1-18; examples 4-6 *	1-19	
P,Y	EP-A-0 556 957 (UNILEVER) * claims 1-18 *	1-19	
			TECHNICAL FIELDS SEARCHED (Int.Cl.5) A61K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	21 March 1994	Willekens, G

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
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E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)